

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte GARRY B. TAKLE and SHAJI T. GEORGE

Appeal No. 2001-1705¹
Application No. 08/616,141

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-8, 11-13, and 19-31. Claims 9 and 10 are free from rejection, and the examiner indicated (Answer, page 2) that claims 14-18 are allowable.

Claim 19 is illustrative of the subject matter on appeal and is reproduced below:

19. A composition for delivering a compound having a net negative charge to cells comprising
 - a. a compound having a net negative charge ionically bound to a macrocycle having a net positive charge selected from the group consisting of natural porphyrins, natural phthalocyanins, synthetic porphyrins, synthetic phthalocyanins, and conjugates

¹ This appeal is related to Appeal No. 2001-1498 (Application No. 08/912,378) accordingly we have considered these two appeals together.

thereof, in an amount effective to enhance delivery of the compound to cells preferentially binding the macrocycle, and

- b. a pharmaceutically acceptable carrier for pharmaceutical administration.

Claim 1 is drawn to a method of using the compound-macrocycle mixture.

In addition, various dependent claims further limit the macrocycle to porphyrin, which may have antiviral activity including, as set forth in claim 26, anti-hepatitis B activity.

The references relied upon by the examiner are:

- Dixon et al. (Dixon) 5,192,788 Mar. 09, 1993
- Leonetti et al. (Leonetti) "Antibody-Targeted Liposomes Containing Oligodeoxyribonucleotides Complementary to Viral RNA Selectively inhibit Viral Replication," Proc. Natl. Acad. Sci., Vol. 87 pp. 2448-2451 (1990)
- Doan et al. (Doan) "Sequence-Targeted Chemical Modification of Nucleic Acids by Complementary Oligonucleotides Covalently Linked to Porphyrins," Nucleic Acids Research, Vol. 15, No. 21 pp. 8643-8658 (1987)
- Korba et al. (Korba) "Use of a Standardized Cell Culture Assay to Assess Activities of Nucleoside Analogs Against Hepatitis B Virus Replication," Antiviral Research, Vol. 19 pp. 55-70 (1992)
- Liszewicz et al. (Liszewicz) "Specific inhibition of human immunodeficiency virus type 1 replication by antisense oligonucleotides : An in vitro model for treatment," Proc. Natl. Acad. Sci., Vol. 89 pp. 11209-11213 (1992)
- Yuan et al. (Yuan) "Targeted Cleavage of mRNA by Human RNase P," Proc. Natl. Acad. Sci., Vol. 89 pp. 8006-8010 (1992)
- Cannon, "Pharmaceutics and Drug Delivery Aspects of Heme and Porphyrin Therapy," Journal of Pharmaceutical Sciences, Vol. 82, No. 5 pp. 435-446 (1993)
- Offensperger et al. (Offensperger) "In vivo Inhibition of Duck Hepatitis B Virus Replication and Gene Expression by Phosphorothioate Modified Antisense Oligodeoxynucleotides," The EMBO Journal, Vol. 12, No. 3 pp. 1257-1262 (1993)

Yu et al. (Yu) "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," Proc. Natl. Acad. Sci, Vol. 90 pp. 6340-6344 (1993)

GROUND OF REJECTION

Claim 31 stands rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the claimed invention.

Claims 1, 2, 5, 6, 19, 20, 23 and 30 stand rejected under 35 U.S.C. § 102(b) as anticipated by Cannon

Claims 1-8, 11, 12, 19-25 and 31 stand rejected under 35 U.S.C. § 103 as being unpatentable over Dixon in view of any one of Yu, Leonetti or Lisiewicz.

Claims 1-8, 11-13, 19-24 and 31 stand rejected under 35 U.S.C. § 103 as being unpatentable over Doan and Offensperger.

Claims 26-29 stand rejected under 35 U.S.C. § 103 as being unpatentable over Dixon, Yuan, Offensperger and Korba.

We reverse.

DISCUSSION

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, a patent application must adequately disclose the claimed invention so as to enable a person skilled in the art to practice the invention at the time the application was filed without undue experimentation. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371-72, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999). We note, however, that "nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is

provided through broad terminology or illustrative examples.” In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). As set forth in In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993):

When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

As the examiner recognizes (Answer, page 5), “[c]laim 31 recites dissociation of the macrocycle from the compound after internalization inside the cells.” As we understand the examiner’s position, since “page 6, lines 9-12 [of the specification], provides support for internalization of the complex within cells, but not for dissociation of the complex”, the specification fails to enable the claimed invention.

Lines 9-12, on page 6 of appellants’ specification state “the compound to be delivered is ionically bound to the macrocyclic compound until it and the bound nucleic acids are internalized in the targeted cells [emphasis added].” According to appellants (Reply Brief, page 3), “[t]he critical term in this passage [is] – ‘until’” This language, absent factual evidence to the contrary, is sufficient to objectively enable the claimed invention. Marzocchi.

What is missing from the examiner’s rejection is factual evidence disputing appellants’ objectively enabled specification. It is the examiner’s burden to make out a case of non-enablement. In our opinion, the examiner has

not met her burden on this record. Accordingly, we reverse the rejection of claim 31 under 35 U.S.C. § 112, first paragraph.

THE REJECTION UNDER 35 U.S.C. § 102:

The following quote represents the examiner's entire statement of rejection under 35 U.S.C. § 102(b). "Claims 1, 2, 5, 6, 19, 20, 23, and 30 stand rejected under 35 U.S.C. [§] 102(b) as being anticipated by Cannon." Answer, page 5. In responding to appellants' arguments (Answer, page 8), the examiner finds:

[t]he instant claims are drawn to compositions comprising a compound having a net negative charge ionically bound to a macrocycle (porphyrin) having a net positive charge and to methods of delivering compounds having a net negative charge to cells comprising mixing the compound with a macrocycle having a net positive charge, wherein the macrocycle ionically binds to the compound.

Conspicuous in its absence in this statement, and the statement of the rejection, is any explanation as to why the amounts in Cannon would be effective to enhance delivery of the compound to cells that bind the macrocycle, as is required by the claimed invention. While the examiner argues (Answer, page 9), "[t]he method of Cannon has the same active steps as the claimed method i.e. the mixing together of a negatively charged compound (lipid) with a positively charged macrocycle ... and the delivery of the mixture to cells" the examiner fails to explain where Cannon teaches an amount that is effective to enhance delivery of the compound to cells as is required by the claimed invention.

"Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim." Gechter v. Davidson,

116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997). “Every element of the claimed invention must be literally present, arranged as in the claim.”

Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Since Cannon fails to teach an amount of a macrocycle effective to enhance delivery of the compound to the cells, Cannon fails to anticipate the claimed invention. Accordingly, we reverse the rejection of claims 1, 2, 5, 6, 19, 20, 23, and 30 under 35 U.S.C. § 102(b) as being anticipated by Cannon.

THE REJECTIONS UNDER 35 U.S.C. § 103:

The combination of Dixon in view of any one of Yu, Leonetti or Lisziewicz:

The examiner finds (Answer, page 5), Dixon “disclose that certain porphyrins inhibit the reverse transcriptase of HIV-1.” In addition, the examiner finds (Answer, page 6), that each of Yu, Leonetti and Lisziewicz “is concerned with inactivation of HIV-1 through the use of oligonucleotides.” Based on these findings, the examiner concludes (id.), “[i]t would have been prima facie obvious ... to have combined the antiviral porphyrins described by Dixon ... with the antiviral oligonucleotides taught by Yu ..., Leonetti ..., or Lisziewicz ... for an improved multi-drug antiviral treatment regimen.” In responding to appellants’

arguments the examiner makes reference (Answer, page 11) to In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980) for the proposition that “[i]t is prima facie obvious to combine two compositions each of which is taught by the prior

art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.”

In addition, the examiner finds (id.) “it would be expected that ionic bonding would enhance the stability of both the compound and the porphyrin in vivo, as is suggested in Cannon....” For the following reasons we are unable to agree with the examiner’s position. As set forth in In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n.3 (CCPA 1970), “[w]here a reference is relied on to support a rejection, whether or not in a ‘minor capacity,’ there would appear to be no excuse for not positively including the reference in the statement of the rejection”, accordingly the examiner’s reliance on Cannon is inappropriate, and we do not include the teachings of Cannon as part of our deliberations on this issue. Furthermore, it appears that the examiner’s position is that ionic bonding would inherently enhance the stability of both the compound and the porphyrin. Inherency, however, is immaterial if, as here, one of ordinary skill in the art would not appreciate or recognize that inherent result. In re Shetty, 566 F.2d 81, 86, 195 USPQ 753, 756 (CCPA 1977).

Stated differently, none of the references relied upon by the examiner recognize that ionic bonding would enhance the stability of both the porphyrin and the oligonucleotides. In addition, the combination of references also fails to suggest an amount of macrocycle effective to enhance delivery of the oligonucleotides to cells binding the macrocycle. See e.g., Brief, pages 12-13.

For these reasons, it is our opinion that the examiner failed to meet her burden² of providing the evidence necessary to support a prima facie case of obviousness. Accordingly, we reverse the rejection of claims 1-8, 11, 12, 19-25 and 31 under 35 U.S.C. § 103 as being unpatentable over Dixon in view of any one of Yu, Leonetti or Lisziewicz.

The combination of Doan and Offensperger:

The examiner finds (Answer, page 6), Doan, “describe oligonucleotide porphyrin conjugates.” In addition, the examiner finds (id.), Offensberger “describe in vivo inhibition of HBV replication wherein antisense oligonucleotides are employed.” Based on this evidence, the examiner concludes (id.), “[i]t would have been prima facie obvious to ... produced porphyrin-anti-HBV antisense oligonucleotide complexes with the reasonable expectation of inhibiting HBV replication.”

As appellants point out (Brief, page 14), in contrast to the claimed invention which requires an ionic bond between the porphyrin and the compound (oligonucleotide), Doan teach covalently linking an oligonucleotide to a porphyrin ring. In responding to appellants’ argument, it appears that the examiner shifts horses and emphasizes (Answer, pages 12-13) that Offensperger:

also teach encapsidation of the oligonucleotides into liposomes for enhanced stability and delivery to target cells and thus provides the suggestion and motivation to ionically bind the porphyrin with a negatively charged compound by teaching enhanced stability and delivery to target cells when the porphyrin is ionically bound to a lipid.

² The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

However, as appellants point out (Reply Brief, page 5), “Offensperger et al. actually discloses inclusion of a cell surface receptor ligand in a liposome containing an oligonucleotide. This is not what is claimed and does not suggest the presently claimed ionic complexes.”

It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion or motivation to lead an inventor to combine those references. Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). On this record we find no suggestion to modify the teachings of Doan with those of Offensperger to obtain the claimed invention which, as appellants point out, require ionic complexes. Accordingly, we reverse the rejection of claims 1-8, 11-13, 19-24 and 31 under 35 U.S.C. § 103 as being unpatentable over Doan and Offensperger.

The combination of Dixon, Yuan, Offensperger and Korba:

The examiner finds (Answer, pages 6-7), Dixon, “teach that certain porphyrins inhibit HIV-1”; Offensberger “describe in vivo inhibition of HBV by antisense oligonucleotides”; Korba “disclose routing testing methods for determining if a compound has activity against HBV”; and Yuan “disclose the parameters necessary for EGS [external guide sequences] in eukaryotic cells.”

However, as discussed supra, we find no suggestion to modify the teachings of Doan with those of Offensperger to obtain the claimed invention which, as appellants point out, require ionic complexes. Yuan and Korba fail to make up for the deficiencies in the combination of Doan and Offensperger.

Accordingly, we reverse the rejection of claims 26-29 under 35 U.S.C. § 103 as being unpatentable over Dixon, Yuan, Offensperger and Korba.

REVERSED

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Administrative Patent Judge)	
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